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EXAMINER

REIDEL, JESSICA L

ART UNIT

PAPER NUMBER

3766

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

## Office Action Summary

Application No.

10/788,906

Applicant(s)

GIROUARD ET AL.

Examiner

Jessica L. Reidel

Art Unit

3766

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 March 2007 and 19 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-149 is/are pending in the application.
- 4a) Of the above claim(s) 4-7, 14-31, 35-38, 45-62 and 79-148 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 8-13, 32-34, 39-44, 63-78 and 149 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 03/12/2007.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 12, 2007 has been entered.
2. Acknowledgement is made of Applicant's Supplemental Response, which was received by the Office on April 19, 2007. Claim 149 is new and has been added. Claims 1-149 are pending. Claims 4-7, 14-31, 35-38, 45-62 and 79-148 were previously withdrawn.

### ***Information Disclosure Statement***

3. The information disclosure statement (IDS) submitted on March 12, 2007 has been acknowledged and is being considered by the Examiner.
4. Applicant should note that the large number of references in the attached IDS (both presently and previously submitted) have been considered by the Examiner in the same manner as other documents in Office search files are considered by the examiner while conducting a search of the prior art in a proper field of search. See MPEP 609.05(b). Applicant is requested to point out any particular references in the IDS which they believe may be of particular relevance to the instant claimed invention in response to this office action.

### ***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 3766

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 1-2, 8, 13, 32-33, 39, 44, 63, 65-67, 71-73 and 149 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soykan et al. (U.S. 2001/0000802) (herein Soykan) in view of Levine et al. (U.S. 2002/0019350) (herein Levine). As to Claims 1-2 and 149, Soykan discloses a system 51 (see Soykan Fig. 5) comprising a subcutaneous electrode array, read as a sensor to sense a physiological signal (i.e. a pseudo-surface ECG) indicative of a predetermined cardiac condition (i.e. ischemia) (see Soykan page 10, paragraph 86) a coil of antenna lead 24, read as a gene regulatory delivery device that emits a regulatory signal (i.e. an RF signal 26) which *indirectly* regulates gene transfer/expression and a stent, read as a gene regulatory delivery device 18 that emits a regulatory signal (i.e. electrical, mechanical, acoustic, thermal, chemical or combinations thereof) which *directly* regulates gene transfer/expression (see Soykan page 4, paragraphs 25-34, page 5, paragraph 43, page 6, paragraphs 44-46, page 8, paragraphs 64 and 69-72 and page 10, paragraph 88).

Soykan further discloses a controller 92 coupled to the sensor (via sense amplifier 53). The controller 92 is electrically connected via RF signal 26 to gene regulatory signal delivery device 18, which emits a regulatory signal for directly effecting gene transfer. Gene regulatory delivery device 18 converts the magnetic field into an electrical signal, which is then used to create an electric field to trigger the release of specific gene sequences or nucleic acids contained in a retroviral vector. The Examiner considers the phrase "electrically connected" to encompass both wired and wireless electrical connections (see Soykan page 2, paragraph 10, page 4, paragraph 28 and page 10, paragraph 88). The controller 92 is also electrically wired to gene

Art Unit: 3766

regulatory signal delivery device (i.e. the coil of antenna lead 24) via antenna lead 24, which emits a regulatory signal (i.e. an RF signal) for indirectly effecting gene transfer/expression (see Soykan Figs. 2-1 and 5 and page 10, paragraph 88). The controller 92 is adapted to control emission of the regulatory signals based on the sensed physiological signal (see Soykan Fig. 2, page 2, paragraphs 9-11, page 3, paragraphs 12-15, page 4, paragraphs 27-28, page 8, paragraph 69, page 9, paragraphs 82-84 and page 10, paragraph 88). Soykan specifies at page 4, paragraph 33 that endothelial cells and fibroblasts, which can be efficiently infected by retroviral vectors in vitro, and then transplanted back into the host to achieve gene transfer/expression in vivo, are particularly preferred (see Soykan page 4, paragraphs 32-34 and page 5, paragraphs 34-43).

Applicant differs from Soykan in that it is not specified that the gene transfer/expression include regulating a transcriptional control element within such a vector where the transcriptional control element is specified to be operably linked to an open reading frame (i.e. an expression cassette or the like). The Examiner considers the use of operably linked promoters for genetic expression to be well known in the art of in vivo gene therapy with Levine being but one example. Levine discloses compositions, methods and gene therapy agents to promote or inhibit angiogenesis in the treatment of peripheral vascular or cardiovascular diseases (such as ischemia) using a transcriptional control element (i.e. promoter or the like) within a vector which is operably linked to an open reading frame (i.e. an expression cassette or the like). Levine further specifies that administering an expression vector, nucleic acid, angiogenic factor or a delivery vehicle to a cell may comprise electroporating and is thus analogous to the invention of Soykan (see Levine Abstract, page 1, paragraphs 8-9 and 12, page 2, paragraphs 12-18, page 4, paragraphs 29-31, page 5, paragraphs 42-43, page 6, paragraphs 47-56, pages 9-15, page 16,

Art Unit: 3766

paragraphs 157-159, page 17, paragraphs 159-165 and page 18, paragraphs 178-179). It would have been obvious to one having ordinary skill in the art to modify the retroviral vectors of Soykan to include a transcriptional control element operably linked to an open reading frame in order to effect gene expression at the level of transcription as taught by Levine to promote or inhibit angiogenesis in the treatment of peripheral vascular and cardiovascular diseases such as ischemia.

7. As to Claim 8, Soykan discloses that the system 51 further comprises circuitry, read as an event detector 57 to detect the predetermined cardiac condition (i.e. ischemia) from the sensed physiological signal (i.e. a pseudo-surface ECG) where the controller 92 of stimulation device 22 is adapted to control the emission of the regulatory signals in response to a detection of the predetermined cardiac event (i.e. onset of ischemia represented by abnormal morphology) (see Soykan Fig. 2, page 3, paragraphs 22-24, page 4, paragraphs 27-28, page 8, paragraph 69, page 9, paragraphs 82-84 and page 10, paragraph 88).

8. As to Claim 13, the sensor of Soykan senses a physiological signal (i.e. a pseudo-surface ECG) indicative of ischemia and the event detector 57 inherently comprises an ischemia detector since it is capable of detecting ischemia from the sensed ECG signal (see Soykan Fig. 2, page 3, paragraphs 22-24, page 4, paragraphs 27-28, page 8, paragraph 69, page 9, paragraphs 82-84 and page 10, paragraph 88).

9. As to Claims 32 and 33, Soykan discloses a system 51 (see Soykan Fig. 5) comprising an implantable stimulation device, read as an implantable medical device system 22 including a subcutaneous electrode array, read as a sensor to sense a physiological signal (i.e. a pseudo-surface ECG) indicative of a predetermined cardiac condition (i.e. ischemia) (see Soykan page

Art Unit: 3766

10, paragraph 86), a RF transmitter and receiver unit, read as an implant telemetry module 55 to receive an external command from an external programming device (see Soykan Fig. 2, page 9, paragraphs 77-78 and 81), and a stent, read as a gene regulatory delivery device 18 that emits a regulatory signal (i.e. electrical, mechanical, acoustic, thermal, chemical or combinations thereof) which directly regulates gene transfer (see Soykan page 4, paragraphs 25-28, page 5, paragraph 43, page 6, paragraphs 44-46, page 8, paragraphs 64 and 69-72 and page 10, paragraph 88). Soykan discloses that the system 51 further comprises circuitry, read as an event detector 57 coupled to controller 92 to detect the predetermined cardiac condition (i.e. ischemia) from the sensed physiological signal (i.e. a pseudo-surface ECG) where the controller 92 of stimulation device 22 is adapted to control the emission of the regulatory signal in response to a detection of the predetermined cardiac event (i.e. onset of ischemia represented by abnormal morphology) via output pulse generator, read as a gene expression control module 74 (see Soykan Fig. 2, page 3, paragraphs 22-24, page 4, paragraphs 27-28, page 8, paragraph 69, page 9, paragraphs 82-84 and page 10, paragraph 88). Soykan further disclose that alternatively the controller 92, which is also coupled to the implant telemetry module 55 (see Soykan Fig. 2), may receive an external command to control the emission of the regulatory signal via the gene expression control module 74 (see Soykan page 4, paragraph 26). Soykan also discloses that the external programming device is a microprocessor device which provides a series of encoded signals to stimulation device 22 by means of a programming head, read as an external telemetry module which transmits radio frequency encoded signals according to a telemetry system or an external patient initiated command to the implant telemetry module 55 (see Soykan page 4, paragraph 26 and page 9, paragraph 78). Soykan specifies that the controller 92 of stimulation device 22 produces

Art Unit: 3766

a radio frequency signal 26 using antenna-lead 24 which is then received by gene regulatory delivery device 18. The gene regulatory delivery device 18 then converts the magnetic field into an electrical signal, which is then used to create an electric field to trigger the release of genes from a retroviral vector (see Soykan page 2, paragraph 10, page 4, paragraph 28 and page 10, paragraph 88). The Examiner considers the phrase “electrically connected” to encompass both wired and wireless electrical connections (see Soykan page 2, paragraph 10, page 4, paragraph 28 and page 10, paragraph 88). Soykan specifies at page 4, paragraph 33 that “endothelial cells and fibroblasts, which can be efficiently infected by retroviral vectors in vitro, and then transplanted back into the host to achieve gene transfer in vivo, are particularly preferred” (see Soykan page 4, paragraphs 32-34 and page 5, paragraphs 34-43).

Applicant differs from Soykan in that it is not specified that the gene transfer/expression include regulating a transcriptional control element within such a vector where the transcriptional control element is specified to be operably linked to an open reading frame (i.e. an expression cassette or the like). The Examiner considers the use of operably linked promoters for genetic expression to be well known in the art of in vivo gene therapy with Levine being but one example. Levine discloses compositions, methods and gene therapy agents to promote or inhibit angiogenesis in the treatment of peripheral vascular or cardiovascular diseases (such as ischemia) using a transcriptional control element (i.e. promoter or the like) within a vector which is operably linked to an open reading frame (i.e. an expression cassette or the like). Levine further specifies that administering an expression vector, nucleic acid, angiogenic factor or a delivery vehicle to a cell may comprise electroporating and is thus analogous to the invention of Soykan (see Levine Abstract, page 1, paragraphs 8-9 and 12, page 2, paragraphs 12-18, page 4,



Art Unit: 3766

paragraphs 29-31, page 5, paragraphs 42-43, page 6, paragraphs 47-56, pages 9-15, page 16, paragraphs 157-159, page 17, paragraphs 159-165 and page 18, paragraphs 178-179). It would have been obvious to one having ordinary skill in the art to modify the retroviral vectors of Soykan to include a transcriptional control element operably linked to an open reading frame in order to effect gene expression at the level of transcription as taught by Levine to promote or inhibit angiogenesis in the treatment of peripheral vascular and cardiovascular diseases such as ischemia.

10. As to Claim 39, Soykan discloses that the event detector 57 detects the predetermined cardiac condition (i.e. ischemia) from the sensed physiological signal (i.e. a pseudo-surface ECG) and that the controller 92 of stimulation device 22 is adapted to control the emission of the regulatory signal in response to a detection of the predetermined cardiac event (i.e. onset of ischemia represented by abnormal morphology) (see Soykan Fig. 2, page 3, paragraphs 22-24, page 4, paragraphs 27-28, page 8, paragraph 69, page 9, paragraphs 82-84 and page 10, paragraph 88).

11. As to Claim 44, the sensor of Soykan senses a physiological signal (i.e. a pseudo-surface ECG) indicative of ischemia and the event detector 57 inherently comprises an ischemia detector since it is capable of detecting ischemia from the sensed ECG signal (see Soykan Fig. 2, page 3, paragraphs 22-24, page 4, paragraphs 27-28, page 8, paragraph 69, page 9, paragraphs 82-84 and page 10, paragraph 88).

12. As to Claim 63, Soykan discloses the current implantable pulse generators, that are well known in the art, may be modified to stimulate the drug-eluting cells in accordance with the teachings of the implantable medical device system 22 such as a wide variety of microprocessor-

Art Unit: 3766

based implantable pacemakers (see Soykan page 9, paragraph 76). It is inherent that the controllers of such pacemakers would provide control of pacing circuitry in conjunction with the emission of the regulatory signal.

13. As to Claim 67, Soykan discloses the current implantable pulse generators, that are well known in the art, may be modified to stimulate the gene transfer in accordance with the teachings of the implantable medical device system 22 such as a wide variety of microprocessor-based implantable defibrillators or cardiovertors (see Soykan page 9, paragraph 76). It is inherent that the controllers of such defibrillators or cardiovertors would provide control of defibrillation/cardioversion circuitry in conjunction with the emission of the regulatory signal.

14. As to Claim 71, Soykan discloses that the implantable medical device system 22 comprises a hermetically sealed enclosure, read as a can to house at least the implant controller 92 and the implant telemetry module 55 (see Soykan Fig. 2 and page 9, paragraph 77).

15. As to Claim 73, Soykan discloses that the subcutaneous electrode array, read as a sensor to sense a physiological signal (i.e. a pseudo-surface ECG) indicative of a predetermined cardiac condition (i.e. ischemia) is external to the hermetically sealed can (see Soykan Fig. 2 and page 10, paragraph 86).

16. As to Claim 65, the previously modified Soykan reference discloses the claimed invention but does not expressly disclose an embodiment where the implantable medical device system 22 further comprises a cardiac resynchronization therapy (CRT) circuit coupled to the implant controller and wherein the implant controller includes a CRT control module adapted to control delivery of CRT in conjunction with the emission of the regulatory signal. It would have been an obvious matter of design choice to a person of ordinary skill in the art to modify the

Art Unit: 3766

system as taught by Soykan in view of Levine with a CRT circuit coupled to the implant controller where the implant controller includes a CRT control module adapted to control delivery of CRT in conjunction with the emission of the regulatory signal, because Applicant has not disclosed that such modification provides an advantage, is used for a particular purpose or solves a stated problem. One of ordinary skill in the art, furthermore, would have expected Applicant's invention to perform equally well with the pacing circuitry, cardioversion circuitry or defibrillation capabilities as taught by Soykan in view of Levine, because it provides suitable integration of the invention with most current implantable pulse generators of the art and since it appears to be an arbitrary design consideration which fails to patentably distinguish over Soykan in view of Levine.

Therefore, it would have been an obvious matter of design choice to modify Soykan in view of Levine to obtain the invention as specified in the claim(s).

17. As to Claim 66, the previously modified Soykan reference discloses the claimed invention but does not expressly disclose an embodiment where the implantable medical device system 22 further comprises a remodeling control (RCT) therapy circuit coupled to the implant controller and wherein the implant controller includes a RCT control module adapted to control delivery of RCT in conjunction with the emission of the regulatory signal. It would have been an obvious matter of design choice to a person of ordinary skill in the art to modify the system as taught by Soykan in view of Levine with a RCT circuit coupled to the implant controller where the implant controller includes a RCT control module adapted to control delivery of RCT in conjunction with the emission of the regulatory signal, because Applicant has not disclosed that such modification provides an advantage, is used for a particular purpose or solves a stated

Art Unit: 3766

problem. One of ordinary skill in the art, furthermore, would have expected Applicant's invention to perform equally well with the pacing circuitry, cardioversion circuitry or defibrillation capabilities as taught by Soykan in view of Levine, because it provides suitable integration of the invention with most current implantable pulse generators of the art and since it appears to be an arbitrary design consideration which fails to patentably distinguish over Soykan in view of Levine.

Therefore, it would have been an obvious matter of design choice to modify Soykan in view of Levine to obtain the invention as specified in the claim(s).

18. As to Claim 72, Soykan discloses the claimed invention but does not expressly disclose an embodiment where hermetically sealed can further houses the sensor. It would have been an obvious matter of design choice to a person of ordinary skill in the art to modify the system as taught by Soykan with the sensor within the can of the implantable medical device system 22, because Applicant has not disclosed that such a location for the sensor provides an advantage, is used for a particular purpose, or solves a stated problem. One of ordinary skill in the art, furthermore, would have expected Applicant's invention to perform equally well with the subcutaneous electrode array, read as a sensor, which is not located within the can of the device as taught by Soykan, because it provides suitable means for detecting a pseudo-surface ECG signal to be input to the device for event detection and since it appears to be an arbitrary design consideration which fails to patentably distinguish over Soykan.

Therefore, it would have been an obvious matter of design choice to modify Soykan to obtain the invention as specified in the claim(s).

Art Unit: 3766

19. Claims 3 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soykan in view of Levine as applied to claims 1 and 32 above, and further in view of Hamm et al. (U.S. 2004/0030379) (herein Hamm). The previously modified Soykan reference discloses that the controller 92 of stimulation device 22 produces a radio frequency signal 26 using antenna-lead 24 which is then received by gene regulatory delivery device 18. The gene regulatory delivery device 18 converts the magnetic field into an electrical signal, which is then used to create an electric field to trigger the release of the transcriptional control element (i.e. promoter or the like) (see Soykan page 2, paragraph 10, page 4, paragraph 28 and page 10, paragraph 88). It is inherent that not all of the magnetic field is transferred into a pure electrical signal and that some electromagnetic field is left/applied for transduction. The previously modified Soykan reference discloses the claimed invention as discussed above except that the amount of electromagnetic field is not predetermined.

Hamm, however, discloses an on demand medical device that includes an electromagnetic field generator for facilitation of transduction to directly or indirectly regulate a regulatable transcriptional control element (see Hamm Abstract, page 1, paragraphs 4-7, page 2, paragraphs 22 and 26 and page 3, paragraphs 26-27). Hamm also discloses that the gene regulatory signal delivery device may be a stent or the like and is thus synonymous with the invention of Soykan (see Hamm page 4, paragraphs 39-40). Hamm further discloses that one skilled in the art can determine the excitation source frequency of the electromagnetic source depending on the size of the molecules being used for delivery and/or the compositions of the gene regulatory signal delivery devices being used (see Hamm page 7, paragraph 86). Therefore, it would have been obvious to one having ordinary skill in the art to modify the system of

Art Unit: 3766

Soykan in view of Levine and Hamm to include an electromagnetic field generator with a generation of a predetermined frequency for the electromagnetic field to tailor the speed of transduction for the particular promoter/transcriptional control element being used in the invention.

20. Claims 9 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soykan in view of Levine as applied to claims 1, 8, 32 and 39 above, and further in view of Darvish et al. (U.S. 2002/0183686) (herein Darvish). The previously modified Soykan reference discloses the claimed invention as discussed above except the event detector 57 is not specified to comprise an event parameter generator to produce one or more condition parameters related to at least one of a type and a degree of the predetermined cardiac condition and the controller 92 is not specified to comprise a regulatory signal parameter controller to quantitatively control the emission of the regulatory signal based on the one or more condition parameters.

Darvish, however, discloses a drug delivery device for targeted release of a molecule (i.e. genetic material) carried in a circulating reservoir comprising at least one electrode 804 and a controller 810 adapted to electrify the electrode 804 with at least one electric field to electroporation or electrical transportation of the molecule. Darvish further discloses that the device is used to control the type, timing and/or dosage of molecule to be applied (see Darvish Abstract, page 1, paragraphs 7-10, page 2, paragraphs 16 and 18-19 and page 3, paragraphs 22-30). Darvish further discloses that the apparatus 100 may comprise a sensor 108 for measuring a physiological parameter (i.e. of the heart 102) and that the controller (i.e. CPU) 122 of the apparatus 100 uses the measurement from the sensor input 130 for determining the parameters of the electrification (see Darvish page 4, paragraph 45 and page 7, paragraph 105). In addition the

apparatus 100 of Darvish further includes a watchdog, which watches over the heart to assure that the heart does not, as a result of the treatment, exceed operational or functional parameters defined by the heart's activity. Specifically, the watchdog is implemented as a separate processor/sensor, which is involved in a feedback loop to stop or modify application of the electric field, read as quantitatively control the emission of a regulatory signal in response to a sensed arrhythmia or ventricular tachycardia, read as one or more condition parameters relating to a type of a predetermined cardiac condition (see Darvish page 7, paragraph 105-108, page 8, paragraph 109, page 13, paragraphs 182-186, page 15, paragraphs 216-217 and page 17, paragraph 243). Darvish discloses that the application regimen may be varied in response to needs of the excitatory tissue (see Darvish page 2, paragraph 19). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the event detector of Soykan in view of Levine and Darvish to comprise an event parameter generator to produce one or more condition parameters related to at least one of a type and a degree of the predetermined cardiac condition and to modify the controller of Soykan in view of Darvish to comprise a regulatory signal parameter controller to quantitatively control the emission of the regulatory signal based on the one or more condition parameters to allow the application regimen to be varied in response to needs of the excitatory tissue.

21. Claims 10-12 and 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soykan in view of Levine as applied to claims 1, 8, 32 and 39 above, and further in view of Donahue et al. (U.S. 2002/0155101) (herein Donahue). The previously modified Soykan reference discloses system 51 (see Soykan Fig. 5) comprising a subcutaneous electrode array, read as a sensor to sense a physiological signal (i.e. a pseudo-surface ECG) indicative of a

Art Unit: 3766

predetermined cardiac condition (i.e. ischemia). It is inherent that the stimulation device 22 comprises an electrogram sensing circuit since it sensed an electrogram from the output the subcutaneous electrode array, read as a sensor. The previously modified Soykan reference discloses the claimed invention as discussed above except that the event detector 57 does not comprise an atrial or ventricular fibrillation detector.

Donahue, however, teaches that it is well known in the art to use a regulatable transcriptional control element in cardiac gene therapy for treatment of any of the following: sinus bradycardia, sinus tachycardia, atrial tachycardia, atrial fibrillation, atrial flutter, atrioventricular nodal block, atrioventricular node reentry tachycardia, atrioventricular reciprocating tachycardia, ventricular tachycardia or ventricular fibrillation (see Donahue page 7, paragraph 94). Donahue also discloses that practice of the invention is broadly compatible with one or a combination of different administration systems (see Donahue page 7, paragraph 88) for more effective and flexible anti-arrhythmic therapies by providing therapeutic methods for administering one or more therapeutic polynucleotides to the heart under conditions sufficient to modulate (increase or decrease) at least one heart electrical property. Donahue further discloses that the invention modulates heart electrical conduction, reconfigures all or part of the cardiac action potential (AP) and reduces or avoids significant disruption of normal electrical function (see Donahue page 2, paragraph 14). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Soykan in view of Levine and Donahue to administer the gene therapy upon detection of an atrial fibrillation or ventricular fibrillation to better the invention's capabilities of eliminating a wide variety of predetermined cardiac conditions.



Art Unit: 3766

22. Claims 64 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soykan in view of Levine as applied to claims 32, 63 and 67 above, and further in view of Shelton et al. (U.S. 5,312,453) (herein Shelton). Applicant differs from the previously modified Soykan reference in that the delivery of pacing pulses or cardioversion/defibrillation shocks is based on at least the external command. The Examiner considers the use of external commands to control pacing/cardioversion/defibrillation delivery to be conventional and well known in the art with Shelton being but one example. Specifically, Soykan discloses that the implantable medical device system 22 disclosed may be incorporated into the rate-responsive pacemaker of Shelton (see Soykan page 9, paragraph 76).

23. Claims 69-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soykan in view of Levine as applied to claims 32, 63 and 67 above, and further in view of Bardy (U.S. 5,314,430). Applicant differs from the previously modified Soykan reference in that the device comprises at least one atrial defibrillation lead coupled to the defibrillation circuit to delivery the defibrillation shocks to one or more atria and the defibrillation control module comprises an atrial defibrillation control module. Applicant also differs from the previously modified Soykan reference in that the device comprises at least one ventricular defibrillation lead coupled to the defibrillation circuit to delivery the defibrillation shocks to one or more ventricles and the defibrillation control module comprises an ventricular defibrillation control module. The Examiner considers the use or atrial/ventricular leads coupled to atrial/defibrillation control modules in a implantable pulse generator/defibrillator to be conventional and well known in the art for the defibrillation of both that atria and ventricles with Bardy being but one example.

Art Unit: 3766

Specifically, Soykan discloses that the implantable medical device system 22 disclosed may be incorporated within the defibrillator of Bardy (see Soykan page 9, paragraph 76).

24. Claims 74-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soykan in view of Levine as applied to claim 321 above, and further in view of Nelson et al. (U.S. 2002/0072785). As to Claim 74, the previously modified Soykan reference discloses that the analog electrogram of the patient's electrical heart activity may be uploaded to the external programming device but does not expressly disclose that the electrogram is displayed (see Soykan page 7, paragraph 83). The previously modified Soykan reference discloses the claimed invention as discussed above except that the external system does not comprise a presentation device to present the sensed physiological signal or a user input to receive the external command. The Examiner considers the use of a presentation device to present the sensed physiological signal, such as an external device including a display and a user input to receive the external command to be conventional and well known in the art with Nelson being but one example (see Nelson page 7, paragraph 58).

25. As to Claim 75, Soykan discloses that the external device is an external programmer (see Soykan page 9, paragraphs 77-78).

26. As to Claims 76-78, Soykan discloses that the external system comprises an advanced patient management system including an external device wirelessly coupled to the implantable medical device system via telemetry (i.e. the external programmer). Soykan discloses the claimed invention as discussed above except that it is not specified that the advanced patient management system also includes a remote device to provide access to the implantable medical device system from a distant location and a network connecting the external device and the

Art Unit: 3766

remote device. The Examiner considers the use of a remote device with a network to be conventional and well known in the art of external programming for implantable medical devices with Nelson being but one example (see Nelson Abstract, Fig. 1, page 1, paragraph 6 and page 4, paragraphs 28-32).

### ***Double Patenting***

27. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Art Unit: 3766

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

28. Claims 1-3, 8-13, 32-34, 39-44, 63-78 and 149 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-109 of copending Application No. 10/890,825 (Amended April 11, 2007). Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are either a broadening of the scope of the patented claims or an obvious variant thereof. Specifically, all the limitations claimed in the current application are expressly presented in the amended claims of copending Application No. 10/890,825.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

29. Claims 1-3, 8-10, 13, 32-34, 39-41, 71-75 and 149 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 13 and 15-18 of copending Application No. 11/220,397. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are either a broadening of the scope of the patented claims or an obvious variant thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

30. Claims 1-3, 8-9, 13, 32-34, 39-40, 44, 63-64, 71-75 and 149 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 11-13 and 16-17 of copending Application No. 11/276,077. Although the conflicting claims

Art Unit: 3766

are not identical, they are not patentably distinct from each other because the current claims are either a broadening of the scope of the patented claims or an obvious variant thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Response to Arguments***

31. Applicant's arguments filed March 12, 2007 and April 19, 2007 have been fully considered but they are not persuasive. In response to Applicant's argument that neither Soykan or Levine teach or suggest a gene regulatory signal delivery device that emits a regulatory signal which directly or indirectly regulates a transcriptional control element, the Examiner respectfully disagrees. As previously discussed, the Examiner interprets the coil of antenna lead 24 to be synonymous with a gene regulatory delivery device that emits a regulatory signal (i.e. an RF signal 26) that *indirectly* regulates gene transfer/expression. The Examiner further interprets the stent to be synonymous with a gene regulatory delivery device 18 that emits a regulatory signal (i.e. electrical, mechanical, acoustic, thermal, chemical or combinations thereof) that *directly* regulates gene transfer/expression (see Soykan page 4, paragraphs 25-28, page 5, paragraph 43, page 6, paragraphs 44-46, page 8, paragraphs 64 and 69-72 and page 10, paragraph 88). Soykan specifically discloses the use of genes or nucleic acids stored within retroviral vectors for electroporation to effect gene transfer. As previously discussed and clarified in this Office Action, Applicant differs from Soykan in that it is not specified that the gene transfer include regulating a transcriptional control element within such a vector where the transcriptional control element is specified to be operably linked to an open reading frame (i.e. an expression cassette or the like). The Examiner considers the use of operably linked promoters for genetic expression to

Art Unit: 3766

be *well known in the art* of in vivo gene therapy with Levine being but *one example* [emphasis added]. Levine discloses compositions, methods and gene therapy agents to promote or inhibit angiogenesis in the treatment of peripheral vascular or cardiovascular diseases (such as ischemia) using a transcriptional control element (i.e. promoter or the like) within a vector which is operably linked to an open reading frame (i.e. an expression cassette or the like). Levine further specifies that administering an expression vector, nucleic acid, angiogenic factor or a delivery vehicle to a cell may comprise electroporating and is thus analogous to the invention of Soykan (see Levine Abstract, page 1, paragraphs 8-9 and 12, page 2, paragraphs 12-18, page 4, paragraphs 29-31, page 5, paragraphs 42-43, page 6, paragraphs 47-56, pages 9-15, page 16, paragraphs 157-159, page 17, paragraphs 159-165 and page 18, paragraphs 178-179). It would have been obvious to one having ordinary skill in the art to modify the retroviral vectors of Soykan to include a transcriptional control element operably linked to an open reading frame in order to effect gene expression at the level of transcription as taught by Levine to promote or inhibit angiogenesis in the treatment of peripheral vascular and cardiovascular diseases such as ischemia.

In response to Applicant's piecemeal analysis of the references, it has been held that one can not show non-obviousness by attacking references individually where, as here, the rejections are based on combinations of references. *In re Keller*, 208 USPQ 871 (CCPA 1981).

### ***Conclusion***

32. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure.

Art Unit: 3766

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica L. Reidel whose telephone number is (571) 272-2129. The examiner can normally be reached on Mon-Thurs 8:00-5:30, every other Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Carl H. Layno can be reached on (571) 272-4949. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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